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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,083	07/13/2001	Timothy I. O'Brien	D6223CIP/C/D	4623

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,083	O'BRIEN, TIMOTHY J.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 30-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25, 27-29 and 32-39 have been cancelled.

Claims 26 and 30 have been amended.

2. Claims 26 and 30-31 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The objections to the disclosure for not containing an updated priority statement and a non-descriptive title are withdrawn in view of the amendments filed 8/30/2004.

6. The objection to claim 27 for failing to further limit the subject matter of a previous claim is withdrawn in view of the cancellation of claim 27.

7. The rejections of claims 26-31, parts a and b, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of the Applicant's arguments and amendments to the claims.

Response to Arguments

8. The rejection of claims 26 and 30-31 under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 8/30/2004 has been carefully considered, but is deemed not to be persuasive. The response states that claim 26 has been amended to recite a SCCE polypeptide that has an amino acid sequence selected from the group consisting of SEQ ID Nos. 31-36, 80, 86 and 99 and a SCCE polypeptide encoded by the DNA of SEQ ID NO:30 and Applicant submits that the specification provides adequate written description showing possession of the recited SCCE polypeptides. In response to this argument, the claims recite that the SCCE polypeptide "has" an amino acid sequence selected from the group consisting of SEQ ID Nos. 31-36, 80, 86 and 99. The term "has" is open claim language (equivalent to comprising), meaning that the 9-mer SCCE peptides of SEQ ID Nos. 31-36, 80, 86 and 99 do not exclude additional amino acid residues either at the N-terminus or C-terminus or both N- and C-termini. Thus, the claims encompass SCCE fragments of any size and undefined structure. The specification does not disclose the full-length SCCE polypeptide sequence nor does the specification disclose any other polypeptide fragment of SCCE that "has" the recited sequences other than SEQ ID Nos. 31-36, 80, 86 and 99. Thus, there is inadequate written description for any SCCE polypeptide that "has" the sequence of SEQ ID Nos. 31-36, 80, 86 or 99, which produce SCCE reactive T cells.

9. The rejection of claims 26 and 30-31 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims is maintained.

The response filed 8/30/2004 has been carefully considered, but is deemed not to be persuasive. The response states that claim 26 has been amended to recite a method of using SCCE polypeptides to produce SCCE-reactive T cells, wherein said SCCE polypeptides include those with amino acid sequences of SEQ ID Nos. 31-36, 80, 86 and 99 and the polypeptide encoded by the DNA of SEQ ID NO:30. The response also argues that the methodology of using peptide-pulsed dendritic cells to generate immune-activated T cells is readily available to one of ordinary skill in the art and in view of the disclosed SCCE polypeptides disclosed in the instant application, one of ordinary skill in the art could practice the claimed invention without undue experimentation. In response to these arguments, while the methodology of using peptide-pulsed dendritic cells to generate immune-activated T cells is readily available to one of ordinary skill in the art, the claims are drawn to a SCCE polypeptide that "has" the amino acid sequence of SEQ ID NO: 31, 32, 33, 34, 35, 36, 80, 86 or 99, which is open claim language and thus, the claims still encompass SCCE fragments of any size and undefined structure. The specification does not teach the amino acid sequence of the full-length human SCCE, the general tolerance to modification and extent of such tolerance and the specification provides insufficient guidance as to which of the essentially infinite possible choices (i.e., SCCE fragments) are likely to be successful. The art of Burgess et al, Lazar et al, Schwartz et al, Lin et al, Lederman et al and Li et al already of record demonstrates that protein chemistry is unpredictable and Applicant did

not address this art in the response filed 8/30/2004. While the declaration of Timothy J. O'Brien filed 2/19/2003 submits that 9-mer peptides corresponding to amino acid residues 5-13 (i.e., SEQ ID NOS:33, 35, 36 and 86) and 123-131 (i.e., SEQ ID NO:32) of human SCCE possess binding motifs of HLA class I molecules and were effective at inducing specific CD8+ CTL responses in vitro, the art of Geysen demonstrates that even for peptides of similar size derived from the same "parent" polypeptide, not all will be capable of interacting with T-cells (column 2, lines 5-9 and Figure 6), thus demonstrating the degree of uncertainty in the art for predicting which subsets or portions of a larger polypeptide will be capable of interacting with or stimulating T-cells. Applicant has not provided any objective evidence demonstrating that the claimed method of producing activated T cells against the innumerable SCCE fragments at issue and has not provided any exemplary method of reintroducing SCCE activated dendritic cells into an individual that has just any cancer, is suspected of having just any cancer or is at risk of getting just any cancer. Although not addressed in the response filed 8/30/2004, the claims still encompass using the full-length human SCCE enzyme and SCCE fragments, which are not necessarily human SCCE fragments for producing activating T cells directed towards SCCE in a human patient that has any cancer, is suspected of having any cancer or is at risk of getting any cancer. The specification teaches that SCCE is expressed in ovarian tumors and the prior art teaches that SCCE is also expressed in prostate cancer. There is no teaching or evidence of record that SCCE is expressed in any type of cancer other than ovarian and prostate. The skilled artisan would not know how to use activated T cells against SCCE to treat just any

cancer, particularly cancers wherein SCCE is not expressed. Further, there is no guidance in applicant's specification to assist the skilled artisan in the selection of an individual at risk of getting a cancer.

10. The rejection of claims 26 and 30-31 under 35 U.S.C. 103(a) as being unpatentable over Paglia et al in view of Cohen et al is maintained.

The response filed 8/30/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that the Paglia et al reference is in contrast to the claimed invention in that Paglia et al teach priming an immune response against MHC class I-restricted antigen by using dendritic cells for presentation of tumor-associated antigens, whereas in the instantly claimed invention dendritic cells are first exposed to SCCE polypeptides to produce activated dendritic cells, which are then used to stimulate T cells to generate SCCE reactive T cells. The response also argues that Cohen et al do not teach the SCCE polypeptides claimed because SEQ ID NO:33 is a protein of 224 amino acids, whereas the present invention recites the use of the full-length SCCE polypeptide or SCCE peptides that are 9 amino acids in length. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With respect to applicant's arguments against Paglia et al, the declaration of Timothy J. O'Brien filed 2/19/2003 submits that human SCCE 9-mer peptides

corresponding to amino acid residues 5-13 and 123-131 possess binding motifs of HLA class I molecules and were effective at inducing specific CD8+ cytotoxic T lymphocyte responses in vitro. The examiner notes that in humans the MHC class I molecule is also called an HLA class I molecule because MHC molecules were first demonstrated on leukocytes. Thus, HLA class I and MHC class I merely represent different names for the same molecule.

With respect to applicant's arguments against Cohen et al, applicant's arguments are not commensurate in scope with the claims. Applicant is reminded that "has" is open claim language as discussed above, meaning that the recited 9-mer SCCE peptides of SEQ ID NOS:31, 32, 34, 80 and 99 encompass additional sequence and therefore reads on the mature SCCE polypeptide of 224 amino acids as taught by Cohen et al (see Figures 3A-1 to 3D-1). Further, due to the indefinite nature of the claims (see item #12 below), SEQ ID NO:30 is interpreted to encode the mature SCCE polypeptide and thus, Cohen et al reads on the claim .

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art . In re McLaughlin, 170 USPQ 209 (CCPA 1971). References are evaluated by what

they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In this case, Paglia et al teach a method of loading dendritic cells in vitro with a tumor antigen and the activated dendritic cells prime cytotoxic T lymphocytes and provide an efficient in vivo immune reaction against tumors (see summary and pages 320-321) and Cohen et al teaches an SCCE polypeptide that has an amino acid sequence selected from SEQ ID Nos:31, 32, 34, 80 or 99 (i.e., the mature SCCE polypeptide encoded by SEQ ID NO:30) as a target for the design of therapeutic treatments for prostate tumors or metastases. Therefore, in view of the combined teachings of Paglia et al and Cohen et al, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the SCCE polypeptide taught by Cohen et al in the method of Paglai et al to prime dendritic cells in vitro (i.e., expose dendritic cells to SCCE) and readminister the activated dendritic cells into a prostate cancer patient, thereby producing activated T cells directed toward SCCE for therapeutic benefit of prostate cancer.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

11. The provisional rejection of claims 26 and 30-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-11 of copending Application No. 10/372,521 is maintained.

The response filed response 8/30/2004 has been carefully considered, but is deemed not to be persuasive. The response states that Applicant submits a terminal

disclaimer to obviate the provisional obviousness-type double patenting rejection, however, no terminal disclaimer has been filed and therefore, the rejection is maintained.

New Grounds of Rejection

12. Claims 26 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26 and 30-31are indefinite for reciting "amino acid sequence encoded by the DNA of SEQ ID NO:30" in claim 26. The prior art of Hansson et al (The Journal of Biological Chemistry, 269(30):19420-19426, 1994) teaches that the full-length human SCCE polypeptide is 253 amino acid residues long and contains a 22-amino acid residue signal peptide and a propeptide of 7 amino acid residues, which are not part of the mature human SCCE protein. It is unclear what polypeptide the DNA sequence of SEQ ID NO:30 encodes because the human SCCE cDNA sequence of SEQ ID NO:30 does not match the nucleotide sequence of human SCCE cDNA taught by Hansson et al, which does encode the human SCCE polypeptide (see Figure 1A). What polypeptide is encoded by SEQ ID NO:30? Further, in view of the teachings of Hansson et al, it is not clear if Applicant is claiming the full-length SCCE polypeptide or are the mature SCCE polypeptide or the SCCE polypeptide lacking the signal peptide.

13. Claims 26 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method of producing activated T cells directed toward SCCE comprising exposing dendritic cells to a SCCE polypeptide that has an amino acid sequence encoded by the DNA of SEQ ID NO:30, thereby activating dendritic cells, and exposing the activated dendritic cells to T cells, thereby producing activated T cells directed toward the SCCE polypeptide and the method encompasses reintroducing the activated dendritic cells into a cancer patient.

The specification does not describe the SCCE protein(s) that is/are encoded by SEQ ID NO:30. The specification discloses a DNA sequence, which is disclosed as encoding the full-length human SCCE protein (see SEQ ID NO:30). The prior art of Hansson et al teaches the nucleotide sequence of human SCCE and the amino acid sequence of the SCCE preproprotein (see Figure 1A). The sequence of SEQ ID NO:30 when compared to the human SCCE sequence taught by Hansson et al deos not appear to be the full length cDNA of human SCCE. For example, SEQ ID NO:30 begins with the sequence 5'-TTGAGGGTTTTGTGTTTCTT-3', whereas the human SCCE sequence of the prior art begins with the sequence 5'-CGGGATTTCCGGGCTCCATG-3'. The specification does not identify or describe the 5' and 3' regulatory regions and untranslated regions of the SCCE sequence, the specification does not identify any

open reading frame of the full-length cDNA of SCCE (SEQ ID NO:30), the specification does not identify the first amino acid or the last amino acid of the SCCE polypeptide encoded by SEQ ID NO:30 and the specification does not disclose the 22-amino acid signal peptide or the 7-amino acid propeptide of the SCCE protein, which are not part of the mature SCCE protein. Again, the specification does not disclose any SCCE polypeptide that is encoded by SEQ ID NO:30, which is disclosed as the full-length cDNA of SCCE.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed SCCE polypeptide, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

Conclusions

14. No claim is allowed.

15. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER